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Original Article

Sleep architecture in school-aged children with primary snoring

Yin Zhu [a,1,*], Chun-Ting Au [a,1], Hugh S. Lam [a,1], Ching-Ching K. Chan [a,1], Crover Ho [b,2], Yun-Kwok Wing [b,2], Albert M. Li [a,1]

[a] Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong
[b] Department of Psychiatry, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong

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ABSTRACT

Objective: We aimed to examine if sleep architecture was altered in school-aged children with primary snoring (PS).
Methods: Children ages 6 to 13 years from 13 primary schools were randomly recruited. A validated obstructive sleep apnea (OSA) screening questionnaire was completed by their parents. Children at high risk for OSA and a randomly chosen low-risk group were invited to undergo overnight polysomnography (PSG) and clinical examination. Participants were classified into healthy controls, PS, mild OSA, and moderate to severe OSA (MS OSA) groups for comparison.
Results: A total of 619 participants underwent PSG (mean age, 10.0 ± 1.8 years; 396 (64.0%) boys; 524 (84.7%) prepubertal). For the cohort as a whole, there were no significant differences in measures of sleep architecture between PS and nonsnoring healthy controls. In the multiple regression model, percentage of nonrapid eye movement (NREM) stage 1 (N1) sleep had a significantly positive association, whereas percentage of slow-wave sleep (SWS) had a significantly negative association with sleep-disordered breathing (SDB) severity after controlling for age, gender, body mass index (BMI) *z* score, and pubertal status. In prepubertal children with PS, no significant disruption of sleep architecture was found. However, pubertal adolescent PS participants had significantly higher adjusted percentage of N1 sleep and wake after sleep onset (WASO) compared to healthy controls.
Conclusions: PS did not exert significant adverse influences on normal sleep architecture in prepubertal school-aged children. Nevertheless, pubertal adolescents with PS had increased N1 sleep and WASO.

1. Introduction

Sleep architecture represents the cyclical pattern of sleep as it shifts between the different sleep stages, including nonrapid eye movement (NREM) and rapid eye movement (REM) sleep. Early in the night, one transitions from lighter sleep stages (NREM stage 1 sleep [N1]) to deeper stages (slow-wave sleep [SWS]), with REM sleep more often appearing during the latter part of the night [1]. Sleep architecture allows us to produce a picture of what an overnight sleep looks like, considering various depths of sleep and arousals to wakefulness. In children, it has been demonstrated that sleep efficiency, percentage of SWS, and REM sleep decreases and percentage of lighter NREM stage 2 (N2) sleep and Tanner stage increases with age [2–4].

Sleep-disordered breathing (SDB) consists of a spectrum of diseases, with severity ranging from primary snoring (PS), upper airway resistance syndrome (UARS), and obstructive sleep apnea (OSA) [5,6]. OSA in school-aged children is associated with both neurocognitive dysfunction and behavioral problems [7,8]. Apart from intermittent hypoxia, sleep fragmentation may account for the demonstrated neurocognitive impairment. Disturbance of normal sleep architecture is one form of sleep fragmentation. Recent scientific research has shown that children with OSA were more likely to have disturbed sleep architecture compared to children with PS or healthy controls, including decreased percentage of SWS [9–11] and REM sleep [11–13], as well as increased percentage of N1 sleep [9,12,14,15] and REM latency [10,15]. Furthermore, these changes were reversible following treatment of OSA [16–18].

PS is defined as snoring in the absence of apnea or hypopnea during sleep [19]. It is positioned at the milder end of the SDB spectrum, and several studies demonstrated that even PS also might exhibit neurobehavioral impairments and cardiovascular morbidities, though the mechanism is unclear [10,20–25]. Snoring is an upper airway breathing sound or noise caused by partial or complete occlusion of the upper airway [26]. Little attention has been

* Corresponding author. Tel.: +852 2632 2917; fax: +852 2636 0020.
E-mail address: jodiezy@163.com (Y. Zhu).
[1] Address: Department of Paediatrics, 6th Floor, Clinical Sciences Building, Prince of Wales Hospital, Shatin, Hong Kong.
[2] Address: Department of Psychiatry, Shatin Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong.

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given to determine if it will disturb normal sleep architecture. The majority of the few published studies have failed to reveal any significant differences in sleep architecture between primary snorers and healthy control participants [10,14,27,28]. Miano et al. [9] found that primary snorers had a higher percentage of N1 sleep and Yang et al. [15] demonstrated increased sleep latency in participants with PS. However, these studies had small sample sizes. Additionally, the SDB groups in the previous studies were recruited from clinics; hence more severe cases may be included and selection bias may exist.

In our study, we aimed to investigate the sleep architecture of school-aged children with PS recruited from the community. We hypothesized that the percentage of certain sleep stage or wakefulness after sleep onset (WASO) in primary snorers would be different from that in nonsnoring healthy controls.

2. Methods

2.1. Participants

Our study was part of our previous research which aimed to investigate the prevalence of OSA in a community-based sample of school-aged children [29]. In brief, participants between the ages of 6 and 13 years were recruited from 13 randomly selected schools. Parents were asked to complete a validated OSA screening questionnaire [30] that stratified children into high or low risk for OSA. All high risk and a selected sample from the low risk group based on a computer-generated random number were invited to undergo overnight polysomnography (PSG) and clinical examination. Children were excluded if they had an intercurrent illness within 4 weeks of PSG; cardiac, renal, or neuromuscular diseases; chromosomal abnormalities; medication which could affect sleep or respiration within 4 weeks of PSG; or previous upper airway surgery. Written informed consent and assent were obtained from the parents and participants, respectively. Approval by the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee was obtained.

2.2. PSG

All recruited children underwent standard overnight PSG at a dedicated sleep laboratory with CNS 1000P polygraph (CNS Inc., Chanhassen, Minnesota, USA). In brief, electroencephalogram (EEG) from four leads (C3/A2, C4/A1, O1/A2, and O2/A1), bilateral electrooculogram, submental electromyogram, bilateral leg electromyogram, and electrocardiogram were recorded. The positions of the participant, respiratory airflow (nasal cannula connected to pressure transducer), thoracic and abdominal respiratory efforts (piezo-based effort belts), arterial oxyhemoglobin saturation (oxygen saturation [SpO2] by Ohmeda 3700 pulse oximeter, Boulder, CO, USA), and snoring sound (microphone) were measured. All data were scored by four PSG technologists and the reports were reviewed and finalized by a chief technologist.

Sleep architecture was scored in 30-s epochs according to the criteria outlined by Rechtschaffen and Kales [31]. The following parameters of sleep architecture were measured: total sleep time (TST), defined as time from sleep onset to the end of the final sleep minus wakefulness after sleep onset; sleep latency, defined as the time occurred from lights out to the first epoch of any sleep; the percentage of each sleep stage out of TST (stage 1, 2, SWS [NREM sleep stages 3 and stage 4], and REM sleep); and WASO, defined as the time spent awake during sleep period time (time from sleep onset to the end of final sleep).

Respiratory events and arousals were scored according to standardized criteria [32]. An obstructive apnea was defined as the absence of airflow with persistent respiratory effort lasting longer than two baseline breaths, irrespective of arterial oxygen saturation changes. An obstructive hypopnea was defined as a reduction of 50% or more in the amplitude of the airflow signal with persistent respiratory effort. It was only quantified if it was longer than two baseline breaths and was associated with oxygen desaturation of at least 4% or arousals. Arousal was defined as an abrupt shift in EEG frequency during sleep, which may include theta, alpha, or frequencies greater than 16 Hz but not spindles of 3 to 15 s in duration. In REM sleep, arousals are only scored when accompanied by concurrent increases in submental electromyogram amplitude. Obstructive apnea–hypopnea index (OAHI) was defined as the total number of obstructive apneic and hypopneic episodes per hour of sleep. Oxygen desaturation index was defined as the total number of dips in arterial oxygen saturation >3% per hour of sleep. The SpO_2 nadir also was noted. Arousal index (ArI) was defined as the total number of arousals per hour of sleep. Participants were classified into four groups according to the PSG and questionnaire results: group 1 was the healthy control group (OAHI < 1 and history of snoring <3 nights per week); group 2 was the PS group (OAHI < 1 and history of snoring $\geqslant$3 nights per week); group 3 was the mild OSA group (OAHI 1–5); and group 4 was the moderate to severe OSA (MS OSA) group (OAHI $\geqslant$ 5).

2.3. Anthropometry assessment

The weight, height, and Tanner stage of all participants were assessed on the day of PSG. Body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Weight, height, and BMI were converted to *z* scores appropriate for age and gender, according to local reference [33]. Pubertal stage was evaluated using a self-assessment questionnaire to categorize Tanner stages [34]. Prepubertal was defined as Tanner stage 1 and pubertal defined as Tanner stage 2 or higher.

2.4. Statistical analyses

All statistical analyses were performed using SPSS 16.0 (SPSS Inc., Chicago, Illinois) and a *P* value <.05 was considered statistically significant. The participants were divided into four groups (healthy controls, PS, mild OSA, and MS OSA) for comparison. The mean (standard deviation [SD]), median (interquartile range), and percentage were presented for parametric, nonparametric, and categorical data, respectively. Parametric with equal variances data were compared using 1-way analysis of variance and the Bonferroni correction was used for post hoc pairwise comparisons ($P < .05$ was statistically significant). Nonparametric and parametric data without equal variances were compared, and the Kruskal–Wallis test and Mann–Whitney tests with adjusted *P* values (significant at $P < .0083$) were used for pairwise comparisons. The χ^2 test was used to assess the differences in proportion between the four groups.

Multiple linear regression analysis was used to assess the relationship between SDB category (control, PS, mild OSA, and MS OSA) and sleep architecture outcomes, controlling for age, gender, BMI *z* score, and puberty status. SDB category, gender, and puberty status were converted to dummy variables (0 for controls, 1 for PS, 2 for mild OSA, and 3 for MS OSA; 0 for girls and 1 for boys; 0 for prepubertal and 1 for pubertal). Residual analysis was performed for each regression model to test the validity of model assumptions.

Analysis of covariance models were used to further examine differences in sleep architecture variables among control, PS, and OSA groups after separately controlling for age, gender, and BMI *z* score in prepubertal and pubertal children. Nonparametric variables were normalized using logarithmic transformation.

Table 1
Demographic and polysomnographic data.

	Controls (n = 248)	PS (n = 104)	Mild OSA (n = 200)	MS OSA (n = 67)	P value
Age (y)[d]	10.0 (1.8)	9.5 (1.8)	10.2 (1.8)	9.8 (1.7)	.005
Men (%)[b,c]	54.4	64.4	71.0	77.6	<.001
BMI[b,c,d,e]	17.5 (3.1)	18.0 (3.3)	19.0 (3.9)	19.7 (3.6)	<.001*
BMI z score[b,c]	0.29 (1.11)	0.59 (0.90)	0.68 (1.08)	0.99 (1.01)	<.001
Puberty (%)	17.7	9.6	17.5	9.0	.088
OAHI (/h)[b,c,d,ef]	0.12 (0–0.49)	0.16 (0–0.48)	1.3 (1.2–2.8)	8.2 (6.5–11.6)	<.001*
SpO_2 nadir (%)[b,c,d,e,f]	93 (92–94)	93 (92–95)	92 (90–93)	90 (88–92)	<.001*
ODI (/h)[b,c,d,e,f]	0.12 (0–0.37)	0.22 (0–0.46)	0.53 (0.23–1.05)	3.04 (1.21–5.51)	<.001*
ArI (/h)[b,c,d,e,f]	5.8 (4.4–7.5)	5.9 (4.4–8.0)	7.0 (5.4–8.4)	10.5 (8.2–14.9)	<.001*
TST (min)	470 (66)	474 (56)	467 (62)	465 (66)	.741
Sleep latency (min)	17.5 (10.5–29.5)	18.3 (10–27.5)	15.5 (9–33.4)	12.5 (6–27.5)	.271*
Stage 1 (%TST)[b,c,d,e]	6.0 (4.4–7.8)	6.0 (4.5–8.1)	7.5 (5.4–9.6)	8.4 (5.6–12.5)	<.001*
Stage 2 (%TST)	48.5 (5.8)	48.7 (5.6)	48.4 (5.2)	47.0 (5.9)	.205
SWS (%TST)	24.2 (6.3)	24.0 (5.5)	22.9 (5.6)	23.1 (4.9)	.108
REM sleep (%TST)	21.0 (4.5)	20.9 (3.7)	20.8 (4.3)	20.2 (4.9)	.579
WASO (%SPT)	8.9 (5.1–13.5)	8.7 (6.3–12.0)	9.0 (5.6–14.8)	9.6 (6.2–13.3)	.451*

Abbreviations: PS, primary snoring; MS OSA, moderate to severe obstructive sleep apnea; y, years; BMI, body mass index; OAHI, obstructive apnea–hypopnea index; SpO_2 nadir, oxygen saturation nadir; ODI, oxygen desaturation index; ArI, arousal index; TST, total sleep time; SWS, slow-wave sleep; REM, rapid eye movement; WASO, wakefulness after sleep onset; SPT, sleep period time.
Mean (standard deviation), median (interquartile range), and percentage (%) are presented for parametric, nonparametric, and categorical data, respectively.
* Kruskal–Wallis test was used.
[a] Significant difference between controls and PS.
[b] Significant difference between controls and mild OSA.
[c] Significant difference between controls and MS OSA.
[d] Significant difference between PS and mild OSA.
[e] Significant difference between PS and MS OSA.
[f] Significant difference between mild OSA and MS OSA.

3. Results

A total of 619 children underwent overnight PSG (mean age, 10.0 ± 1.8 years; 396 (64.0%) boys; 524 (84.7%) prepubertal). The demographic and polysomnographic characteristics of the participants with different SDB severities are compared in Table 1. The proportion of boys and BMI z score increased across the four groups. As expected, significant differences in OAHI, SpO_2 nadir, oxygen desaturation index, and ArI were found across groups, except between controls and participants with PS. For sleep architecture parameters, mild and MS OSA group had significantly higher percentage of N1 sleep compared to the controls and PS group. However, there were no significant differences in measures of sleep architecture between the PS and control group.

In all of the measures of sleep architecture, N1 sleep (%TST) had a significantly positive association after controlling for age, gender, BMI z score, and puberty status; however, SWS (%TST) had a significantly negative association with SDB categories ranging from healthy controls, PS, and mild to MS OSA. As expected, age and puberty status exerted an effect on sleep architecture (Table 2).

We further divided the whole cohort into prepubertal and pubertal participants and compared the sleep architecture measures between controls, PS, and OSA groups, respectively, after adjusting for age, gender, and BMI z score. The proportion of boys was significantly different between prepubertal and pubertal groups (68.3% vs 40.0%; P < .001). This finding may be because girls typically enter the pubertal stage earlier than boys. The sample size was 204 controls (94 PS and 226 OSA in prepubertal children) and 43 controls (11 PS and 41 OSA in pubertal children).

We found that N1 sleep (%TST) and SWS (%TST) were significantly different between healthy controls and children with PS and OSA in the prepubertal subgroup. Additionally, N1 sleep (%TST), and natural logarithm of WASO (percentage of sleep period time [%SPT]) were significantly different between SDB severity categories in the pubertal subgroup. Nevertheless, the significantly higher percentage of N1 sleep and lower percentage of SWS were only present between the OSA and non-OSA group (control or PS) in prepubertal children. The differences between control participants and PS did not reach statistical significance. However, significantly increased N1 sleep (%TST) and natural logarithm of WASO (%SPT) existed between OSA and non-OSA group but also between PS and control group in pubertal children (Fig. 1A–D).

4. Discussion

In our large community-based study, no significant disruption of sleep architecture was found in children ages 6–13 years with PS when compared to nonsnoring healthy children. After controlling for age, gender, BMI z score, and puberty status, increased

Table 2
Significant predictor variables in the multiple regression model for the association between the sleep architecture and sleep-disordered breathing category (controls, primary snoring, mild obstructive sleep apnea, and moderate to severe obstructive sleep apnea) adjusted for age, gender, body mass index z score, and puberty (N = 619).

Outcome variable	Predictor variable	β	95% CI	Standard error	P value
Stage 1%TST	SDB category	0.91	0.65–1.17	0.13	<.001
	Age	0.39	0.21–0.56	0.09	<.001
	BMI z score	0.33	0.08–0.59	0.13	.012
SWS%TST	SDB category	−0.62	−1.04 to −0.19	0.22	.004
	Age	−0.81	−1.10 to −0.53	0.15	<.001
	Puberty	−1.79	−3.24 to −0.33	0.74	.016

Abbreviations: CI, confidence interval; TST, total sleep time; SDB, sleep-disordered breathing; BMI, body mass index; SWS, slow-wave sleep.

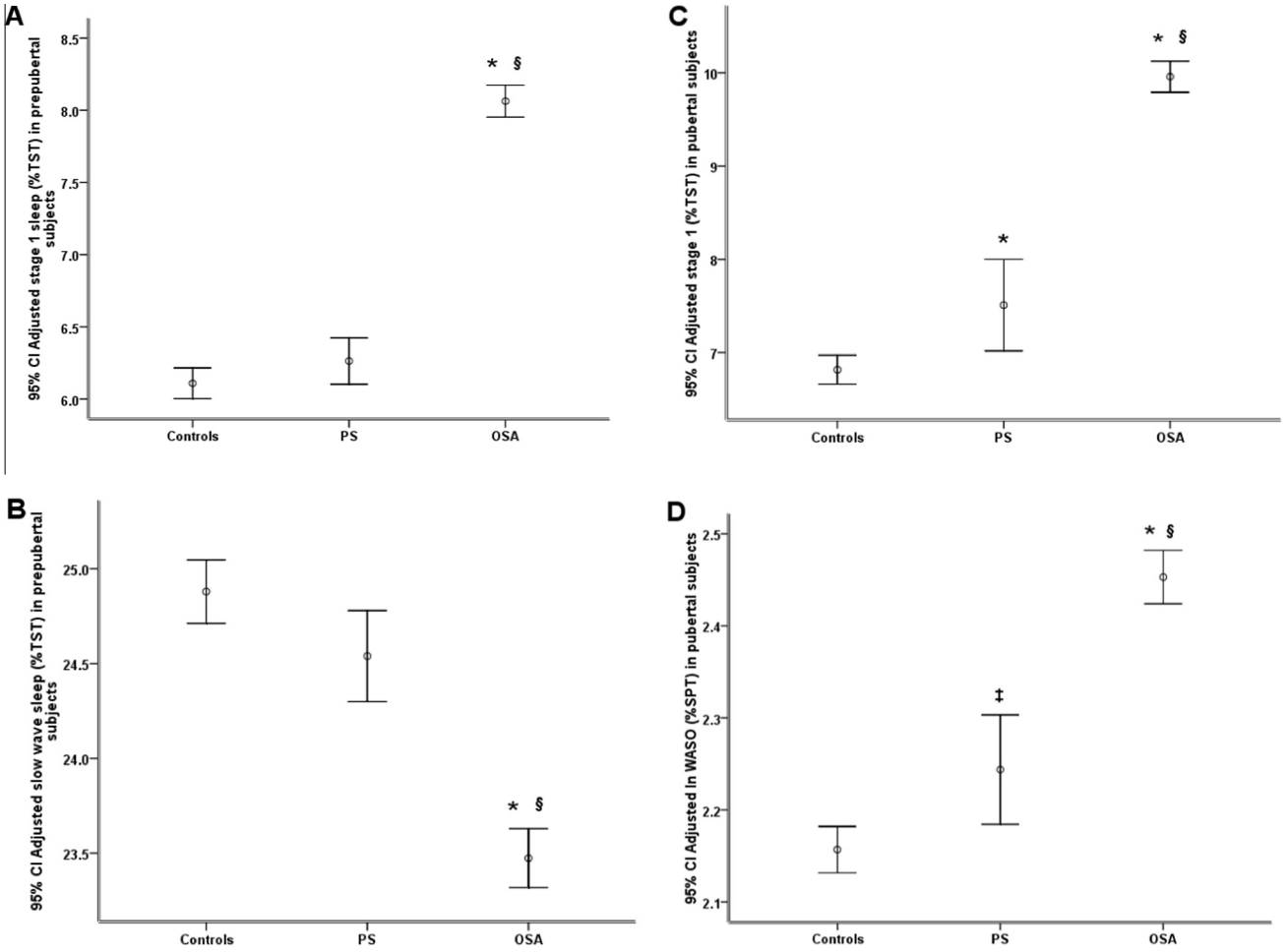

Fig. 1. A–D. The Fig. shows the means with 95% confidence intervals of nonrapid eye movement sleep stage 1 (N1) in prepubertal participants, slow-wave sleep in prepubertal participants, N1 sleep in pubertal participants, and ln wake after sleep onset in pubertal participants, respectively, adjusted for age, gender, and body mass index *z* score. $^{*}P < .01$ compared with controls. $^{‡}P < .05$ compared with controls. $^{§}P < .01$ compared with primary snoring.

Table 3
Comparison of our findings and previous studies on sleep architecture of primary snoring in children.

Author	Nation	Age (y)	Sample size of PS	Sample size of normal controls	Scoring rule	Difference in sleep architecture between PS and controls
Bourke et al. [14] (2011)	Australia	7–12	59	35	R&K [31]	Not significant
Beebe et al. [27] (2004)	United States	6–12	17	17	R&K	Not significant
Khadra et al. [28] (2008)	United States	7–13	32	14	R&K	Not significant
Miano et al. [10] (2011)	Italy	8.6 ± 1.9	13	60	AASM [1]	Not significant
Yang et al. [15] (2010)	Australia	7–12	50	30	R&K	PS had longer sleep latency
Miano et al. [9] (2010)	Italy	6.2 ± 3.2	26	10	R&K	R&K: not significant
					AASM	AASM: PS had higher N1%

Abbreviations: y, years; PS, primary snoring; R&K, Rechtschaffen and Kales; AASM, American Academy of Sleep Medicine; N1%, percentage of nonrapid eye movement sleep stage 1.

percentage of N1 sleep and decreased percentage of SWS were independently associated with SDB severity in the healthy controls, PS, mild OSA, and MS OSA groups. In prepubertal children, there were no significant differences in adjusted sleep architecture between PS and healthy participants. However, adjusted percentage of N1 sleep and WASO were both significantly elevated in primary snorers compared to nonsnoring participants in pubertal children.

In general, our findings were consistent with published literature comparing PS with nonsnoring healthy controls (Table 3) (i.e., sleep architecture was not impaired in school-aged children with PS until the condition progressed to the development of OSA), especially in prepubertal children. However, even PS participants demonstrated impaired sleep architecture, including higher N1 sleep and WASO in pubertal adolescents. N1 sleep is light sleep most often occurring in the transition from wakefulness to the other sleep stages or following body movements during sleep. If movement arousals occur, N2 or REM sleep is likely to change to N1 sleep according to Rechtschaffen and Kales scoring rules [31]. Therefore, the elevation of N1 sleep was possibly due to cortical or movement arousals and WASO. Although the ArI in the PS and healthy control groups was not significantly different in our data, it is possible that snoring on its own can cause subtle microarousals, which potentially can cause sleep architecture abnormalities

in PS participants. There are a few studies supporting this assumption. An adult study showed that snoring sounds could influence cortical EEG during sleep as evaluated by respiratory cycle-related electroencephalographic changes, which could be modulated by using earplugs [35]. Children who had nonapneic–hypopneic snoring could present with an abnormal sleep EEG, as evidenced by a significant increase in cyclic alternating pattern rates [36].

Studies examining why pubertal adolescents were more prone to have disruption of sleep architecture than prepubertal children were lacking. It is known that adults have more arousals or wakefulness than children [37], suggesting that the threshold of arousals might decrease with age. We also found that WASO (%SPT) was significantly higher in pubertal adolescents compared to prepubertal children (11.2 [SD, 6.6–16.7] vs 8.6 [SD, 5.4–12.9]; $P = .002$). It remains unclear if sexual hormone changes occurring in puberty might have an impact on arousal or awakening during sleep; however, the answer might be negative based on the results of our study, as gender presumably did not have a significant effect on sleep architecture indicated by its absence from Table 2 as a predictor variable. Additionally, there were no significant differences in arousal index, WASO, or sleep stage percentage between pubertal boys and girls according to our data. Hence it is suggested that the change in threshold of arousal with age may be not associated with the sexual hormone change during puberty. The small sample size of pubertal participants in our study could have led to wider variations and less statistical power; thus future studies exploring the effect of puberty on sleep architecture in SDB are still needed.

Evidence showed that higher percentage of N1 sleep adversely impacted learning and memory in children [38]. Increased WASO represented reduced sleep efficiency. A study conducted in healthy adults by our research group showed that lower sleep efficiency was correlated with higher 24-h urinary catecholamines suggesting increased sympathetic activity, which plays a critical role in the pathogenesis mediating cardiovascular complications [39]. SWS facilitated the assimilation of new knowledge [_ENREF_3940] and higher percentages of SWS were associated with better neurocognitive functioning [27]. Thus the significantly increased percentage of N1 and WASO, as well as the trend in reduction in percentage of SWS found in our study, may explain some of the neurocognitive deficits and cardiovascular morbidities seen in children with PS.

There were two limitations in our study. First, esophageal pressure monitoring was not used, and thus cases with UARS may have been missed. Nevertheless, nasal pressure was monitored in our study, which made up for this potential source of error to some extent. Moreover, no significant differences in ArI between healthy participants and the PS participants were found in our study. Second, subtle EEG changes might not have been detected with our conventional monitoring. More sophisticated techniques such as spectral analysis of EEG frequency [40] and cyclic alternating pattern of NREM [41] or REM sleep density [42] are needed to understand more subtle sleep architecture changes in participants with PS.

5. Conclusion

In our study, PS did not exert significant adverse influences on normal sleep architecture in prepubertal school-aged children. Nevertheless, pubertal adolescents with PS had higher N1 sleep and WASO than nonsnoring healthy controls. Because impaired sleep architecture may be related to neurocognitive and cardiovascular consequences, PS should not be considered completely benign. Searching for an appropriate intervention for children with PS may be helpful in future studies.

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2013.08.801.

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